different fungal species – that inhibit centrosomal clustering and thus force tumor cells with supernumerary centrosomes to undergo multipolar mitoses and consequently apoptosis.
Results: This approach led to the identification of several substances which are currently characterized in more detail. One of these substances is the well-known antifungal drug griseofulvin, which, in addition to its inhibition of centrosomal clustering described here, has recently been shown to suppress microtubule dynamic instability.
Conclusion: Taken together, this screening may help identify new potential anti-cancer drugs.

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P47. RADIOPROTECTION OF NORMAL TISSUE CELLS BY TRANSFER OF THE HUMAN SUPEROXIDE-DISMUTASE GENE

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Background: Protection of normal tissue against radiation-induced damage would increase the therapeutic ratio of radiotherapy. A promising strategy for this approach is gene therapy-mediated overexpression of copper–zinc (CuZnSOD) and manganese superoxide-dismutase (MnSOD). Recombinant adeno-associated virus 2 (rAAV2) are attractive vectors owing to their ability to infect non-dividing cells and a very low risk of insertional mutagenesis. The purpose was to test the radio-modulating effects of SOD on human primary lung fibroblasts (HPLF).
Methods: Low passage HPLF (MRC5) cells were transduced with the rAAV2-SOD vectors, harvested on day 3, irradiated (1–8 Gy) and analysed using FACS, Western blot, SOD-activity and colony formation assays.
Results: High transduction rates were obtained with >80% of the HPLF cells expressing the respective SOD. Compared to transduction controls, CuZnSOD did not exhibit any radioprotective effects, whereas for MnSOD-transduced HPLF an increase of approximately 30% in the survival of colony-forming cells was observed (1–4 Gy).
Conclusion: An increase in clonogenic survival (1.3-fold) of HPLF cells after transfer of MnSOD and subsequent irradiation was shown. Earlier, we have shown lack of protection in tumour cells (HeLa), thus supporting that MnSOD may increase the therapeutic ratio. rAAV2 vectors are promising tools for the delivery of radio-protective genes in normal tissue such as the lung for pulmonary or intestine cells for prostate irradiation.

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P48. GONADOTROPHIN RELEASING HORMONE BASED VACCINE (GnRHm1-TT), AN EFFECTIVE CANDIDATE FOR HORMONEDEPENDENT CANCER IMMUNOTHERAPY

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Background: The normal development and functioning of the prostate gland, as well as its benign and neoplastic growth is dependent of androgen. Previous studies with Gonadotrophin Realeasing Hormone (GnRH/LHRH) vaccines, have shown the usefulness of immunization against this hormone in prostate and breast cancer.
Methods: In this work we have designed a vaccine candidate called GnRHm1-TT based on a completely synthetic immunogen. The peptide was formulated as a white semiviscous water in oil preparation and injected to animals.
Results: In healthy animals, this vaccine candidate showed to be very immunogenic, resulting in high anti-GnRH antibodies titers, testosterone reduction and significant decrease of the prostate and testicle weight. In tumor implanted rats the vaccine candidate had demonstrated to produce significant tumor growth inhibition of Dunning R3327-H androgen responsive prostate tumor in rats $P = 0.025$ and survival increase, $P = 0.001$.
Conclusion: GnRHm1-TT have demonstrated to be highly immunogenic and safe, causing prostate and testicle atrophy and significantly tumor growth inhibition. These results make our vaccine candidate useful as an effective androgen deprivation therapy, and possible application to prostate cancer and other hormone-dependent malignancies therapy.

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P49. ZOLEDRONIC ACID HAS DIRECT ANTI-PROLIFERATIVE AND ANTI-METASTATIC EFFECT ON PANCREATIC CARCINOMA CELLS AND ACTS AS AN ANTIGEN FOR δ2 γ/δ T CELLS

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Background: Beside their use as anti resorptive drug, bisphosphonates are well known to stimulate γδ T cells and to have direct effects on tumor growth.
Methods: We determined the direct cytotoxic effect of pamidronate and zoledronic acid, the induction of apoptosis and their anti-metastatic potential. Next, we analyzed how bisphosphonates act on γδ T cells propagated with our recently published protocol. The susceptibility of pancreatic carcinoma cells pretreated with bisphosphonates against γδ T cells was tested in cytotoxicity assays and the subgroup involved in killing was investigated.